Developing Vaccines against Respiratory Syncytial Virus Infection

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Respiratory syncytial virus (RSV) is a major cause of severe lower respiratory tract disease in infancy and early childhood. Despite its importance as a pathogen, there is no licensed vaccine against RSV. The F and G glycoprotein of RSV are potentially important targets for protective antiviral immune responses. Here, recombinant replication-deficient adenovirus-based vaccines, rAd/3xG, expressing the soluble core domain of G glycoprotein (amino acids 131 to 230), engineered by codon optimization and tandem repetition for higher level expression, were constructed and evaluated for their potential as RSV vaccine in murine model. Strong serum IgG as well as mucosal IgA responses were induced by intranasal immunization of rAd/3xG. A single intranasal immunization of rAd/3xG vaccines provided potent protection against RSV challenge without vaccine-enhanced immunopathology. We also tested the efficacy of our vaccines against RSV field isolates from Korean pediatric patients and the data showed that our vaccine confers complete protection against RSV-A isolate challenge. We also show that sublingual or intranasal immunization of a procaryotically expressed and purified G protein fragment of amino acids from 131 to 230, designated Gcf, induces strong serum IgG and mucosal IgA responses. Interestingly, these antibody responses could be elicited by Gcf even in the absence of any adjuvant, indicating a novel self-adjuvanting property of our vaccine candidate. Gcf exhibited potent chemotactic activity in *in vitro* cell migration assay and cysteine residues are necessary for chemotactic activity and self-adjuvanticity of Gcf *in vivo*. Mucosal immunization with Gcf also provides protection against RSV challenge without any significant lung eosinophilia or vaccine-induced weight loss. Together, our data demonstrate that mucosal administration of our vaccine candidates elicit beneficial protective immunity and represent promising vaccine regimens preventing RSV infection.

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Human Anthrax Vaccine Development in Korea National Institute of Health

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Anthrax has been considered one of most likely bio-warfare weapons. It's potential use as an agent of bio-terrorism was highlighted in 2001 by a series of postal mailing attacks in United States. Anthrax is a highly lethal infectious disease caused by the spore-forming bacterium *Bacillus anthracis*. After entering the host, anthrax spores germinate inside macrophages, which transport the bacteria to regional lymph nodes. Released bacilli then multiply extracellularly, secrete high levels of exotoxins, and spread systemically in the bloodstream. The exotoxin is composed of three distinct proteins, protective antigen (PA), edema factor (EF), and lethal factor (LF), which are secreted separately as nontoxic monomers. The binding of LF or EF to PA results in formation of active lethal toxin or edema toxin, respectively, which causes massive edema and organ failure. Among these toxin proteins, because PA can elicit a protective immune response against both anthrax toxins, it is the target antigen of existing anthrax vaccines. Current human anthrax vaccines available in the US and Europe consist of alum-precipitated supernatant material from cultures of a toxigenic, nonencapsulated strain of *B. anthracis*. The major component of human anthrax vaccine that confers protection is PA. A second generation human vaccine using the recombinant PA is being developed.
In 2002, Korea National Institute of Health (KNIH) started to develop human anthrax vaccine for national stockpiling against an emergency situation, The developing vaccine is a second generation vaccine of which major component is a purified recombinant PA. For a mass production of the PA from *B. anthracis,* KNIH established an expression system with *Bacillus brevis* - pNU212 and developed functional assays and animal models for vaccine efficacy tests. With the cooperation of a private sector, Green Cross Co., the development of manufacturing process, preclinical and clinical trial phase I studies were completed. In 2011, clinical trial phase II study will be started in Seoul National Hospital, Seoul Korea. After clinical studies, KNIH is planning to receive a conditional licensure from Korea Food and Drug Administration and to start stockpiling of this vaccine for emergency use.

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Implication of Biochips in Tuberculosis Diagnostics

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To prevent the spreading of tuberculosis, it is necessary to have efficient and prompt methods of detection of the causative agent. Recently, only molecular methods provide rapid (less than 24 h) detection of *M.tuberculosis* with simultaneous determination of pathogen susceptibility to anti-TB drugs. Among existing molecular methods, hydrogel-based biological microchips (biochips) developed at Engelhardt Institute of Molecular Biology proved to be a reliable diagnostic tool.
The biochip used in the system TB-BIOCHIP MDR contains oligonucleotide probes for the detection of IS6110 sequence, as well as probes for the detection of mutations in the gene *rpoB* responsible for resistance to rifampin and in the genes *katG*, *inhA*, and *ahpC*, which cause resistance to isoniazide. The procedure of genome analysis of the TB causative agent using the method is based on hybridization of amplified fluorescently labeled fragments of the aforementioned genes with sets of complementary probes immobilized on biochips.
In the Russian Federation, the TB-BIOCHIP MDR test underwent appropriate certification and was included in routine laboratory diagnostics. It has been used successfully by more than twenty anti-TB institutions. A total of more than 20,000 clinical samples were analyzed with the reported